ΑD				

Award Number: W81XWH-11-2-0082

TITLE: Rehabilitation of Visual and Perceptual Dysfunction after Severe Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: Eliezer Peli

CONTRACTING ORGANIZATION: Schepens Eye Research Institute

Boston, MA 02114

REPORT DATE: May 2014

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command

Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;

Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently

valid OMB control number. PLEASE DO NOT RETUR	RN YOUR FORM TO THE ABOVE ADDRESS.	
1. REPORT DATE (DD-MM-YYYY)	2. REPORT TYPE	3. DATES COVERED (From - To)
May 2014	Final report	01 March 2011-28 February 2014
4. TITLE AND SUBTITLE		5a. CONTRACT NUMBER
Rehabilitation of Visual and Percept	tual Dysfunction after Severe Traumatic Brain Injury	
		5b. GRANT NUMBER
		W81XWH-11-2-0082
		5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	stain Cong Luc Varin Houston and Matter Tomasi	5d. PROJECT NUMBER
Alex Bowers, Ell Pell, Robert Golds	stein, Gang Luo, Kevin Houston and Matteo Tomasi	
		5e. TASK NUMBER
		5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAM	ME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT
		NUMBER
Schepens Eye Research In	stitute	
Boston MA 02114		
 SPONSORING / MONITORING AGEN U.S. Army Medical Research and Materia 		10. SPONSOR/MONITOR'S ACRONYM(S)
Fort Detrick,		
Maryland 21702-5012		11. SPONSOR/MONITOR'S REPORT NUMBER(S)
12. DISTRIBUTION / AVAILABILITY ST	ATEMENT	•

Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT The overall aim was to conduct preliminary evaluations of a new rehabilitation strategy and new functional assessment methods for homonymous hemianopia (HH) and spatial neglect (SN), disabling visual and cognitive perception conditions that commonly occur as a result of severe traumatic brain injury (TBI) and stroke. Both HH and SN prevent detection of objects on the affected side, resulting in unsafe walking and driving. Using realistic tasks in virtual environments representative of everyday mobility challenges we evaluated a novel optical device – expansion prism (EP) glasses - combined with a new computerized perceptual-motor training regimen in helping people with HH and SN detect and avoid obstacles on the affected side. In the first year we developed the training software and prepared the functional assessments. In the second and third years we made excellent progress in recruiting and running participants, with a total of 40 participants screened and 24 enrolled. There were at least 15 visits per participant (total about 50 hours), including about 6 visits for intensive computerized perceptual-motor training. Preliminary results are encouraging. After training there were significant improvements in the ability to accurately touch targets presented in areas of prism-expanded vision in the blind hemifield. Before training, the error in touching was 18° , which reduced significantly (p = 0.007) to only 2.0° after training (equivalent to seeing side accuracy). Blind side detection performance improved significantly with the prism glasses from median 35% without glasses at baseline to 50% with glasses before training (p = 0.003). There was a further improvement to 80% after training (p = 0.028), which was maintained at 3 months (88%).

15. SUBJECT TERMS

Hemianopia; spatial neglect; prismatic corrections; adaptation; perceptual-motor training; rehabilitation: mobility: functional outcome measures

16. SECURITY CLASSIFICATION OF:		17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC	
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U	טט	36	19b. TELEPHONE NUMBER (include area code)

Table of Contents

	Page
Introduction	. 3
Body	4
Key Research Accomplishments	12
Reportable Outcomes	12
Conclusion	13
Bibliography	14
List of personnel	14
Appendices	15

INTRODUCTION

Rehabilitation of Visual and Perceptual Dysfunction after Severe Traumatic Brain Injury

The aim of our project was to conduct preliminary evaluations of new rehabilitation strategies and new functional assessment methods for homonymous hemianopia (HH) and spatial neglect (SN), disabling visual and cognitive perception conditions that commonly occur as a result of severe traumatic brain injury (TBI) and stroke. Both HH and SN prevent detection of objects on the affected side, resulting in unsafe walking and driving. In our pilot study we evaluated a novel optical device combined with a new computerized perceptualmotor training regimen in helping people with HH and SN detect and avoid obstacles on the affected side. The optical device, expansion prism (EP) glasses, uses high power prism segments embedded in a regular spectacle lens to project areas from the affected (blind/neglected) side onto the unaffected (seeing) side while leaving central vision uninterrupted. The purpose of the perceptual-motor training is to help people learn how to interpret the information from the peripheral prisms so that they can correctly identify the location of objects detected via the prisms and respond appropriately (e.g., avoid a collision when walking or turn to face a person approaching on the blind/neglected side). The effects of the EP glasses and training were evaluated using realistic tasks representative of everyday mobility challenges including detection of pedestrian hazards in a driving simulator and obstacle collision judgments in a virtual mall. In addition, this project addressed another important basic research question; namely, the effect of the interventions on eye movement behaviors. Eye movements were measured without and with EP glasses and after training in the driving simulator, the collision judgment task and a natural walking task. The eye movement data provide a basic understanding of how participants were using the device and will help guide future developments of prismatic devices for HH and SN.

Our original statement of work was for 2 years. We were granted a no cost extension for an additional year so that we could complete data collection for the main pilot study.

BODY

I. Task 1 - Preparation of study protocols.

This task was completed in year 1.

II. Task 2 - Complete development of the perceptual-motor training program

This task was mostly conducted and completed in year 1. However, throughout years 2 and 3 we continued to add additional enhancements to the program, fixes to previously hidden bugs, and modifications to allow greater flexibility and ease of use, and improve the more complex aspects of the training.

Accomplishments

- We developed a training program that includes five levels of training 1) proprioceptive-motor adaptation of the prism side hand, 2) discrimination of prism and seeing side targets, 3) increasing speed through elimination of side-pointing strategies, 4) improving resiliency of adaptation using increasing cognitive load, and 5) transferring adaptation into extrapersonal visual space by requiring attention to background scene information.
- Please see the appended draft manuscript for full details of the development of the training program.
- The program has been used extensively in training sessions for the main pilot study (Task 5).

III. Task 3 - Preparation of functional assessments in the driving simulator and virtual mall

In year 1 we completed the modification and testing of existing scenarios in the driving simulator (detection of potential pedestrian hazards) and the existing collision judgment task in the virtual-mall walking simulator. In years 2 and 3, both the driving simulator and virtual mall tasks were successfully deployed in the main pilot study.

Accomplishments - Driving simulator

- We modified software (previously developed for other studies) to analyze detection performance (detection rates, reaction times, and the proportion of pedestrian appearances for which there would have been a collision in the real world), lane position and steering behaviors in the driving simulator.
- We implemented extensive calibration tests and verification procedures for the SmartEye eye and head tracking system used to record eye and head movements when driving with and without prism glasses (so that we can determine how participants are using the EP glasses and the effects of perceptual-motor training on eye movement behaviors).
- We also made excellent progress on developing an algorithm to quantify gaze (eye + head) movement behaviors in the driving simulator; the algorithm is now in the final stages of development.

Accomplishments - Virtual mall walking simulator

- We added new features to the existing collision judgment program to make it suitable for this project.
- We developed data consolidation programs and also data analysis programs, including a new algorithm to analyze collision responses that cannot be fit by a cumulative Gaussian. (Such data were common for HH participants on the side of their field loss).

IV. Task 4 - Development of outdoor walking task, including eye and head tracking

At the beginning of year 2 we purchased a PositiveScience eye tracker and associated software and by the end of the first quarter in year 2 had implemented it in the main pilot study.

Accomplishments

- We completed setting up the Positive Science eye tracker and two separate motion sensors for recording of head position relative to the body when walking, developed calibration procedures, finalized two outdoor walking routes, received training from an orientation and mobility specialist, and collected eye and head position data from all participants in the pilot study.
- We developed a method of integrating the eye and head movement data so that we can analyze scanning behaviors based on gaze direction.

V. Task 5- Pilot study EP glasses and training

Our main focus in years 2 and 3 was on recruiting and running participants in the pilot study which involved 15 to 19 visits per participant, for a total contact time of about 50 hours per participant. Participants were fitted with permanent 57 prism diopter EP glasses in the oblique configuration. Before training commenced, they wore the prism glasses at home for 2 weeks to become accustomed to the glasses. They then received 6 training visits over a 3-week period during which they progressed through the five levels of the training protocol. Performance on the functional assessment test battery was evaluated without prism glasses at baseline, and then with the prism glasses on 3 occasions, after wearing the glasses for 2 weeks (but before training), immediately after training and then again after 3 months. The test battery included collision judgments in the virtual walking simulator, detection performance in the driving simulator and gaze behaviors during outdoor walking.

Enrollment

The original aim was to have 12 patients with HH without SN and 12 patients with HH with SN complete the pilot study. Allowing for attrition, a total of 15 patients with HH without SN and 15 patients with HH with SN were approved for participation. In April 2013, we reached our original recruitment goal of 15 participants for the cohort with HH without SN. We subsequently submitted a request to our local IRB to increase the number of participants with hemianopia without neglect by 4, to a total of 19; the request was approved on 14 May 2013. Thus a total of 19 patients with hemianopia without neglect and 15 patients with hemianopia with neglect were approved for participation.

- A total of 35 patients with HH without SN were screened for the main pilot study, of which 19 met the criteria and were enrolled; 13 have now completed the protocol and 6 withdrew. (The reasons for withdrawal included: too many visits, health issues, moved away from Boston and transportation issues.)
- A total of 5 patients with HH with SN were screened and enrolled in the main pilot study of which 2 have completed the study, 1 is partway through the protocol, 1 withdrew, and 1 was lost to follow-up. Unfortunately we encountered difficulties with recruiting participants with SN due to their generally poorer physical condition than the HH participants without SN and their concerns about the large number of study visits they would have to attend.

Enrollment for each protocol since the start of the study:

Schepens IRB protocol number	HRPO Log Number	Hemianopia Without neglect	Hemianopia With neglect
2011-07 (Prism Training)	A-16638.1	19	5
2011-09 (Eye movements outdoors)	A-16638.2	12	3
2011-010 (Virtual walking sim)	A-16638.3	17	3
2011-011 (Driving sim)	A-16638.4	14	3

Preliminary data

Below we report preliminary data analyses for each of the main aspects of the pilot study.

Please note that all of the results reported in the following sections are unpublished and should be protected.

A. Perceptual Motor Training

Training was conducted with participants sitting about 45cm from a touch screen while wearing the EP prism glasses. The primary training task involved reaching out and touching (on a touch screen) peripheral stimuli displayed on the blind/neglected side and on the seeing side of the visual field while maintaining fixation on a central target (Figure 1). Please see the appended draft paper for full details of the training and training protocol.

None of the 3 participants with HH and SN could be trained with fixed gaze. Because of their attentional impairment, they were unable to maintain their gaze while reaching for the stimulus. Instead, we required them to hold fixation on the central target until the stimulus was detected, and then look (foveate through the carrier) to the actual stimulus location and touch it. Only one subject became consistently accurate with this training from 16° error pre-training to -0.4° error post-training.

We conducted a preliminary analysis of the horizontal touch error data for the 13 participants with HH without SN who have completed the full training protocol (Figure 2). Before training, median horizontal touch error was 18° when reaching to touch targets presented in areas of prism expanded vision (i.e., the majority of participants touched the apparent location of the prism image rather than the true location). This error reduced significantly (p = 0.007) to only 2.0° at the end of training (equivalent to seeing side accuracy). 11/13 patients became accurate with the training and the other 2 showed essentially no improvement. At the 3 month follow-

up, of the 11 patients that improved, 4 retained the full effects of training (touch within 4° of the true target location) whereas the others had partial or total regression back to pre-training levels of touch accuracy.

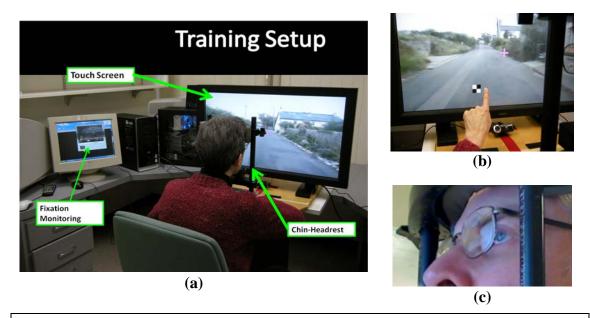


Figure 1: Computerized perceptual motor training

(a) The training station includes a padded antimicrobial forehead rest, wide screen touch monitor, fixation monitoring camera, and operator's station. (b) Patient reaches out to touch the peripheral target (black and white checkerboard square) on a natural driving scene background while fixating the central pink cross. (c) Close up of patient in the forehead rest wearing peripheral prism glasses.

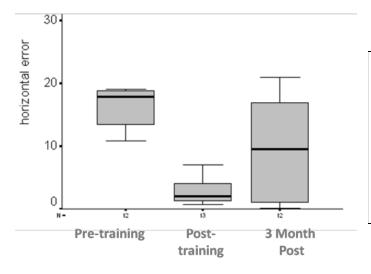
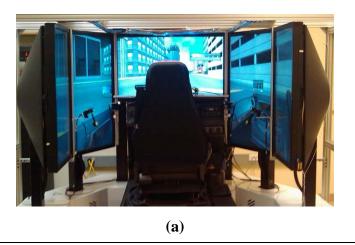


Figure 2: Perceptual-motor training results for 13 participants with HH without SN: median horizontal touch error (in degrees) for targets presented in the prism zones pre-training, immediately post-training, and 3 months after training. There was a significant improvement in accuracy immediately post-training (p = 0.007) and 4 subjects retained the full effects of training after 3 months. The thick black line within the box represents the median; box length represents the interquartile range; whiskers are 1.5x the interquartile range.

B. Driving simulator

Each driving simulator assessment comprised five test drives (each about 10 minutes) on pre-determined routes guided by computer-generated, spoken navigation cues (similar to GPS instructions) (Figure 3a). While driving, the participant's primary task was to press the horn button whenever he/she detected a pedestrian figure that appeared periodically at small and large eccentricities on the right and left of the roadway (Figure 3b). The pedestrian figures (n = 52 in each assessment) moved with biological motion toward the road on a collision course, but did not enter the travel lane. The driving was highly engaging as there was other traffic on the roads and the participants had to obey all the normal rules of the road. Main outcome measures were detection rates and reaction times.



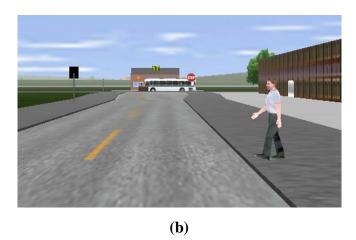


Figure 3: (a) The driving simulator has 5 large LCD screens with 225° horizontal field of view and all the controls in an automatic transmission car. **(b)** Screenshot showing a pedestrian walking toward the road as the participant's vehicle approaches (central monitor only).

Of the three participants with HH and SN that participated in driving simulator sessions, two showed an improvement in blind side detection rates with the prism glasses and one did not (Figure 4).

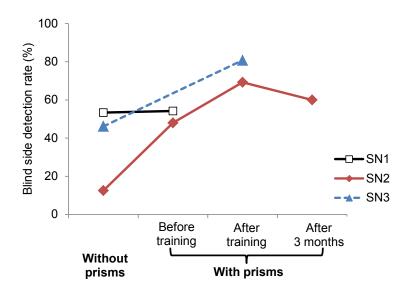
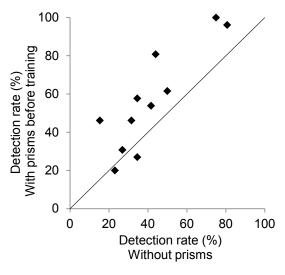
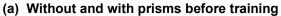
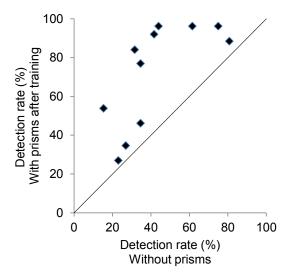


Figure 4: Blind side detection rates for three participants with HH and SN. Two showed an improvement in detection rates with the prism glasses and one did not.

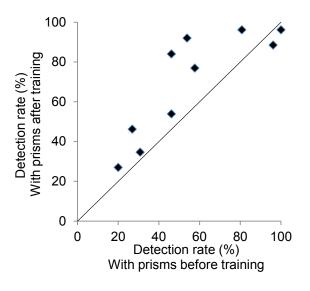
Preliminary analysis of the results for 11 participants with HH without SN indicate a significant improvement in detection of blind side pedestrian hazards with prism glasses and training. Median detection rates improved from 35% without prism glasses to 50% with prism glasses before training (p = 0.003), and further improved to 80% with prism glasses after training (p = 0.003) (Figure 5). The improvement in detection rates with training was significant (p = 0.028) and was maintained at the 3-month follow up (88%, p = 0.57). There was also a significant improvement in reaction times with the prism glasses from median 3.0s without prism glasses to 2.3s with prism glasses before training (p = 0.026). Reaction times did not improve further with training (2.4s) but were maintained at the 3-month follow up (2.4s). Seeing side detection performance (100% and 1.2 s) was significantly better than blind side performance even after training (p = 0.005).



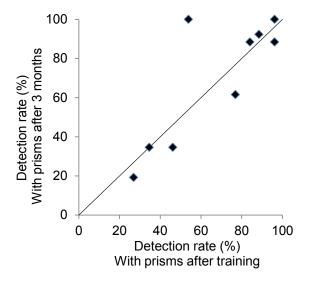




(b) Without prisms before training and with prisms after training



(c) With prisms before and after training



(d) With prism glasses immediately after training and after 3 months

Figure 5: Detection rates for blind side pedestrian hazards for participants with HH without SN.

(a) and (b): Detection rates were better with than without prism glasses. (c) Detection rates improved with training. (d) Improvements immediately following training were retained at the 3 month follow up. (Points above the diagonal represent improvement).

C. Collision judgments in virtual mall walking simulator

Participants were seated with their head in a headrest 100 cm from a wide (94 × 79°) rear-projection screen displaying a video model of an actual shopping-mall corridor (Figure 6). The animated mall corridor generated an optic flow background at 1.5m/sec along a straight path similar to that experienced during actual locomotion. Their task was to report whether they would collide with stationary obstacles (life-sized human figures; Figure 6) that periodically appeared at different offsets (up to 120cm to each side) from the simulated participant's walking direction. Participants performed the task under 4 different conditions: 1) gaze fixed centrally without prisms, 2) gaze fixed centrally with prisms, 3) scanning naturally without prisms, and 4) scanning naturally with prisms.

Blind side detection rates of the three participants with HH with SN showed some improvements with prism glasses in the natural scanning conditions. S1's detection did not improve with prism glasses before training (63% with prisms and 70% without prisms). However, immediately after training, blind side detection was marginally better with the prisms (78% without and 85% with). At the 3 month follow up, blind side detection was significantly better with the prisms (60% without and 88% with). S2 showed good detection even without p-prisms (93% over 3 visits); however, with p-prisms detection was 100% at all assessments, even without any training. S3 has only been measured pre-training. Blind side detection improved markedly from 15% without p-prisms to 100% with p-prisms.

Blind side detection rates of the participants with HH without SN were significantly better with than without the prism glasses in the fixed gaze conditions (improved by 59% with prism glasses, p = 0.01). In addition, under natural scanning conditions, detection rates also increased with the prism glasses (by 18%) to a median of 100%. When wearing the prism glasses, detection rates on the blind side were as good as those on the seeing side.

To evaluate collision judgment performance, a sensitivity index (d-prime) was computed. D-prime compares the observed response to an expected response pattern. An "expected" collision judgment response was derived for each participant by combining all the seeing side data, typically 15 data sets collected over 4 visits. The d-prime was computed for the prism and seeing side data for each individual session (expected was mirrored over to calculate the prism-side d-prime). Thus far, preliminary analyses have been conducted to determine the effects of training on collision judgments with prisms in the fixed gaze condition for 10 participants with HH without SN. The fixed gaze condition with prisms was administered when the prisms were first dispensed, after two weeks of general wear, and then post-training. There was a borderline significant improvement in d-prime from baseline to post training (Wilcoxon, p=0.04). Data from the 3 month post-training session has also been collected, but has not yet been processed. Analyses have not yet been conducted for the free gaze conditions.

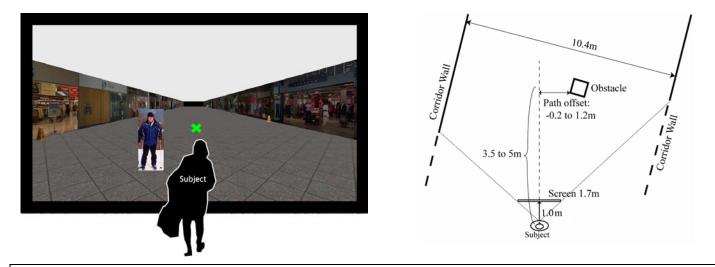


Figure 6. The virtual shopping mall set-up and collision judgment task.

Participants were instructed to fixate a cross at the center of the screen (green x) and imagine that they were walking in a real shopping mall. A figure appeared, moved on a linear path, and disappeared after 1 second. At the end of each trial the participant responded verbally "collision", "no collision", or "nothing". The figure could appear at a range of eccentricity offsets to the right or left of center, or not at all (10% of trials). There were a total of 88 trials.

D. Eye and head movements when walking outdoors

Because of the lack of commercially-available mobile gaze tracking systems which can record both head and eye movements in outdoor situations, we developed our own gaze (head + eye) tracker system using off-the-shelf components. The system (Figure 7) consists of a PositiveScience portable eye tracker and a pair of motion sensors to measure head movements relative to body heading direction. Before data collection with subjects we performed exhaustive tests with the developed system to quantify the system error by comparison to ground

truth data. As head and eye movement data are recorded separately, they have to be synchronized during post-processing. For this purpose we developed customized software that:

- Converted the eye movement data to visual angles
- Synchronized the two data streams and combined them into a gaze (head + eye) output
- Removed unreliable values
- Classified and quantified gaze movements on the blind side and seeing side





(b)

Figure 7: (a) The mobile gaze tracking system including i) two motion sensors to measure head position relative to body position, ii) the Positive Science eye tracker iii) two small notebook computers for data recording. (b) Close up of the eye tracker cameras mounted on a custom frame suitable for the mounting of prism lenses.

Figure 8 shows an example of the output for the gaze (head+eye) and head tracking after the post-processing. To derive the gaze position (red line in Figure 8), the eye movement data were synchronized and added to the head position information (blue line in Figure 8). The plot shows the gaze and head positions in visual angles as a function of time (seconds): positive values represent the points to the right of the heading direction and negatives to the left. In the same plot we also show those points that we classified as fixations based on gaze movement speed: all those gaze points for which the speed was lower than 15°/sec and situated in the far periphery (more than 30°) were defined as fixation points: the green crosses represent the left gaze fixation points and the black the right ones. The number of fixations on each side provides a comparison between blind and seeing sides in terms of the time that gaze was in each hemi field. We analyzed the percentage of gaze fixations exceeding specific visual directions (e.g., >20°, >30°, >40°) relative to primary body and eye position, respectively, using repeated-measures ANOVAs to evaluate the effects of side (seeing/blind) and prism (with/without).

We have collected data for 9 of the subjects with HH without SN. Each participant walked short pre-determined outdoor routes on busy downtown Boston streets. We found that they looked toward the far periphery (at least 30° from their body heading direction) on the blind side significantly more often than toward the seeing side (7.2% of total valid samples vs. 5.7%, p = 0.049; data pooled for with and without prisms conditions). However, the number of gaze fixations to the far periphery was lower when wearing the prisms compared to the without-prisms condition on the blind (6.7% vs 7.7%, p > 0.05) and seeing side (4.7% vs 6.7%, p = 0.018). These preliminary results suggest that hemianopes make larger compensatory gaze scanning movements towards the

far periphery on their blind than their seeing side. However, they make fewer scans to the far peripheral region with the prism glasses than without. This effect was also found on the seeing side and, in fact, the effect on the seeing side was larger. These data suggest both a beneficial effect of the prism expansion on the blind side, as well as a possible shift of attention from the seeing side to the blind side when using the prism glasses.

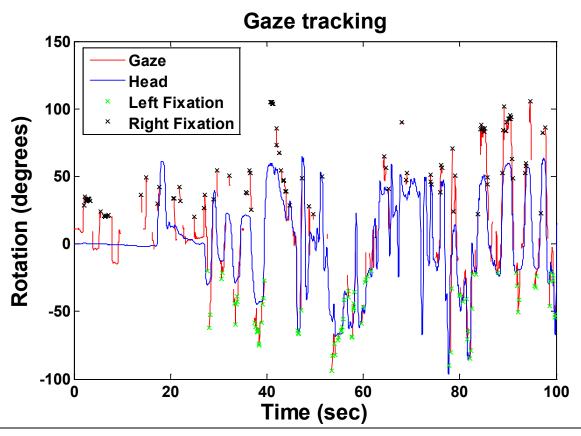


Figure 8. Example of gaze data collected during one of the assessments. For the sake of clarity we report only a small portion (100 seconds) of the full walk. The blue line represents the head rotation and the red line gaze direction.

KEY RESEARCH ACCOMPLISHMENTS

- Development of a comprehensive perceptual-motor training tool, training protocol and data analysis suite;
- Strong evidence of improvement in blindside detection performance with prism glasses and training that is maintained 3 months after the end of training in participants with HH without SN.
- Pilot data from participants with HH with SN (to our knowledge the first such data) which will provide preliminary data for future grant applications;
- Data that establishes our driving simulator pedestrian detection task and virtual mall collision judgment task as good tools for the evaluation of functional performance of patients with HH (both without and with SN)
- Development of a novel algorithm to provide detailed quantification of the gaze scanning behaviors of patients with HH in the driving simulator
- Development of novel methodology for measuring both head and eye position when walking in an outdoor environment and integrating the two sets of data to provide gaze position.

REPORTABLE OUTCOMES

Conference presentations (peer-reviewed abstracts)

- Preliminary results for the virtual-mall walking-simulator collision detection task were presented at the American Academy of Optometry 2012 meeting.
- Preliminary data from the prism training and pre- and post-training results from the virtual-mall walking-simulator collision detection task were presented at ARVO 2013 (Association for Research in Vision and Ophthalmology).
- Early eye and head position data from the outdoor walking task were presented at ARVO 2013
- An abstract reporting final results for the virtual-mall walking-simulator collision detection task for patients without prism glasses has been selected for the Members-in-Training best poster contest at ARVO 2014
- An abstract reporting prism effects and training effects in the driving simulator detection data has been accepted as a talk at ARVO 2014
- An abstract reporting preliminary analysis of the gaze data from the outdoor walking task has been accepted as a poster at ARVO 2014.
- An abstract reporting prism effects and training effects in the driving simulator detection data will be submitted for the annual American Congress of Rehabilitation Medicine.

Invited talks

- Dr Houston gave an invited talk at the New England College of Optometry about the methodology and early results from the study
- Dr Luo's postdoctoral fellow, Matteo Tomasi, gave a talk at Schepens about the development of the outdoor eye and head tracking methodology and preliminary results
- Dr Bowers gave an invited talk at The Eye, The Brain, & The Auto 2013 International Conference that included preliminary data from the driving simulator aspects of the study
- Drs Houston and Bowers gave an invited talk at an in-house training session for staff at Spaulding Rehabilitation Hospital
- Dr Bowers is giving an invited talk about peripheral prism glasses for hemianopia at Vision 2014, The 11th
 International Conference on Low Vision, Melbourne, Australia; the talk will report data from the driving
 simulator aspects of the project.

Papers

- A paper addressing the development of the prism-training methodology is in revision
- A paper reporting data from the collision judgment task in the virtual-mall walking-simulator without peripheral prism glasses is also almost ready for submission
- A paper reporting data from the collision judgment task with peripheral prism glasses is well advanced
- A paper addressing the methodology for integrating eye and head movement data from the outdoor walking task is well advanced
- Other papers reporting the training results and the driving simulator results are in preparation.

CONCLUSIONS

The large number of visits per subject made this study very time intensive both for participants and study team members. The voluminous and complex data posed significant challenges in terms of data integration and development of data analysis programs. Despite these hurdles we made excellent progress on all aspects of the project with a full cohort of participants with HH without SN completing the study.

Our preliminary analyses suggest that, at the end of training, the majority of participants were able to accurately touch the true location of objects presented in the prism zones. In the driving simulator, we measured both an effect of the prisms and an effect of the training: blind side detection rates improved with the prism glasses even

before training and there was further improvement at the end of training, which was maintained at the 3-month follow up. These driving simulator results are very encouraging.

In the simulated walking collision judgment task, the prism glasses also improved the ability of participants to detect potential collision objects on the blind side when using information from the prism image alone (i.e., without scanning to foveate the object). However, preliminary analyses suggest only a marginal improvement in their ability to correctly determine the likelihood of colliding with the detected object using information from the prism image alone.

The data from the outdoor walking task demonstrate our ability to obtain reliable data on gaze behaviors with and without prism glasses. This is an important methodological advance in gaze tracking in unconstrained naturalistic tasks, which will make it possible to evaluate a number of rehabilitation techniques and methods that purport to improve gaze scanning behaviors.

Overall, our results provide strong preliminary data to underpin a randomized controlled clinical trial of the efficacy of peripheral prism glasses and perceptual-motor training for HH. Our data clearly demonstrate that we have the tools to evaluate the functionality of the peripheral prism glasses in a critical clinical trial that will be based not merely on self-reported benefit but on quantitative functional evaluations relevant to important activities of daily living. Such a clinical trial is sorely needed in this area, as highlighted in a number of recent reviews of treatment options for patients with HH (without and with SN). Our preliminary results for HH participants with SN are also important as they suggest that the same approach for treatment and evidence-based evaluation may be applied to SN, which has much more severe consequences for soldiers or veterans impacted by traumatic brain injury than just HH without SN.

BIBLIOGRAPHY

Conference abstracts

Houston KE, Churchill J, Luo G, Russell L. Woods RL, Peli E, Bowers AR. (2012) Peripheral prism glasses for hemianopia improve obstacle detection during virtual walking. Optom. Vis. Sci. 89; E-abstract 120979

Houston KE, Churchill J, Wiegand J, Peli E, Luo G, Goldstein RB, Woods RL, Bowers AR. (2013) Perceptual-motor adaptation in hemianopes wearing peripheral prisms is possible: Preliminary results. Invest. Ophthalmol. Vis. Sci. 54, ARVO E-Abstract 2759.

Tomasi M, Churchill J, Wiegand JP, Houston Kevin; Peli Eli, Bowers AR, Luo G. (2013) Peripheral prisms increase blindside eye and head scanning movements during outdoor walking in hemianopes: preliminary results. Invest. Ophthalmol. Vis. Sci. 54, ARVO E-Abstract 2758.

Bowers AR Houston KE Goldstein RB Peli E. (2014) Peripheral prisms and training improve detection of pedestrians by drivers with hemianopia Invest. Ophthalmol. Vis. Sci. ARVO abstract *accepted*

Houston KE, Liu R, Sheldon S, Peli E, Goldstein RB, Luo G, Woods RL, Bowers AR (2014) Biased Collision Judgments by People with Left but not Right Hemianopia Invest. Ophthalmol. Vis. Sci. ARVO abstract *accepted*

Tomasi M, Bowers AR Peli E Luo G (2014) Compensatory gaze scanning by patients with hemianopia during outdoor walking Invest. Ophthalmol. Vis. Sci. ARVO abstract *accepted*

PERSONNEL

The following personnel received pay from this grant:
Concetta Alberti
Egor Ananev
Doris Apfelbaum
Alex Bowers
Matt Bronstad
Junxiang Chen

Jeffrey Curchhill Christina Gambacorta Robert Goldstein Daejoon Hwang Gang Luo Eli Peli Frank Rogers Qu Tang Sarah Sheldon Lauren Spano Jean Paul Wiegand

In addition, Kevin Houston OD also contributed significantly to the project. He was supported by a K-12 clinician scientist training grant.

APPENDICES

A draft paper describing the development of the prism training software and protocol is appended. The paper will be submitted to Ophthalmic and Physiological Optics within the next week.

DRAFT PAPER

Development of a Protocol for Perceptual-Motor Training for Use with Peripheral Prisms for Hemianopia

Authors: Kevin E. Houston, ¹ Alex R Bowers, ¹ Xianping Fu, ^{1,2} Robert B. Goldstein, ¹ Jeff Churchill, ¹ Jean-Paul Wiegand, ¹ Tim Soo, ¹ Qu Tang, ¹ and Eli Peli ¹

Affiliations:

1 Schepens Eye Research Institute, Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, MA

2 Information Science and Technology College, Dalian Maritime University, Dalian, China

Acknowledgements

Supported in part by DoD grant DM090420 (EP&AB), NIH Grant R01EY12890 (EP), and NIH K12EY016335 (KH) The authors thank Christina Gambacorta and Nicole Ross for assistance in testing early versions of the training program.

Conflict of Interest Disclosures: Dr Peli has financial interest in a patent related to the peripheral prism glasses (assigned to Schepens Eye Research Institute).

ABSTRACT

Purpose: Computerized perceptual-motor training methods for patients with homonymous hemianopia (HH) learning to use peripheral prisms (p-prisms) were developed in preparation for an early-phase clinical study to evaluate preliminary feasibility and efficacy.

Methods: The training methods aim to improve pointing accuracy for peripheral targets appearing in prism expansion areas while gaze is fixed centrally. The following goals are addressed in five training levels over six 1-hour visits: 1) proprioceptive-motor adaptation of the prism side hand, 2) discrimination of prism and seeing side targets, 3) increasing speed through elimination of side-pointing strategies, 4) maintain performance scores under increasing cognitive load, and 5) transferring adaptation into extrapersonal visual space by requiring attention to background scene information. This protocol is being used in an ongoing pilot study of the training to determine preliminary efficacy and transfer to everyday mobility tasks, the results of which will be published in a later manuscript.

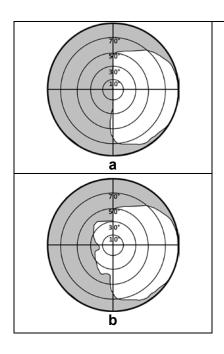
Results: A total of 19 patients were enrolled from July 2011- November 2013, of which 5 withdrew (health=2, attendance=3). Of those who completed or are receiving training (n=14) mean age was 51, 79% male, 100% Caucasian, 64% with left HH.

Conclusions: The software and training protocol are functional and are being used in the ongoing pilot study.

Key Words: Prism, Peripheral Prisms, Peli Lens, hemianopia, hemianopsia, quadranopia, vision rehabilitation, stroke, brain injury, training, prism adaptation

INTRODUCTION

Peripheral prism glasses (p-prisms; also known as EP-glasses or the Peli Lens) provide immediate visual field expansion for patients with homonymous hemianopia (HH), measurable with standard perimetry. The unilateral fitting allows the prism eye to have areas of the seeing hemifield substituted with the prism-shifted views while the fellow eye continues to see the portions of the field obscured by the prisms due to the optical apical scotomas, resulting in true field expansion under binocular viewing conditions. The prisms are PMMA Fresnel segments embedded unilaterally in the lens over the eye on the side of the HH (fig 1) above and below the line of sight. In recent years the p-prism design was improved by increasing the prism power from 40Δ to 57Δ and orienting the bases obliquely (slightly down in the upper segment, and slightly up in the lower segment), providing expansion of the paracentral field (fig 1). P-prisms are limited to the peripheral (superior and inferior) lens (fig. 1) but span both sides of the pupil, and thus also expand the visual field when gazing to the seeing side and to a lesser extent when scanning to the blind side. In clinical trials, between 41% and 83% of patients were still wearing the p-prism glasses after 6 months, reporting improved mobility.



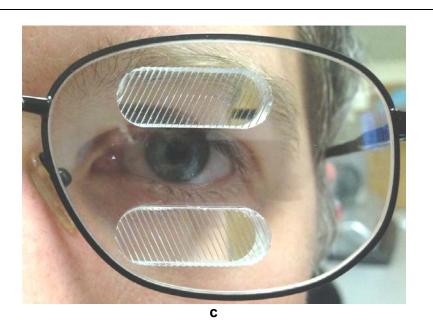


Figure 1 a) The binocular visual field of a patient with left HH as measured by Goldmann Perimetry with V4e stimulus. b) The binocular field of the same patient wearing oblique 57Δ p-prisms. c) The oblique design in the permanent p-prism fitted unilaterally over the left eye as for the patient in 1b. P-prisms are fitted equidistant from the pupil center assuming a ~10° downward gaze when walking (primary gaze is illustrated here).

Although p-prisms immediately expand the visual field upon application (fig. 1a & b), objects on the blind side are perceived as though they are on the seeing side (fig. 2a). We expected patients to show motor and perhaps perceptual adaptation to the prisms with extended wear times, as had been reported by Kohler⁸ and replicated by Pick⁹ for split field prisms, which are optically similar to p-prisms. However, in an earlier study, no motor adaptation was evident after 2-3 months of wear (mean 9 weeks, 4hrs/day).¹⁰

Adaptation to prisms (yoked, dove, and split-field) have reportedly been faster and more complete when combined with an active movement task (ie. reaching) such that physical contact was made with targets viewed through the prism.^{8, 11, 12} With p-prisms, patients are taught to first make an eye movement within the prism-free portion of the lens to the true position of the object prior to making a motor response. Coming into physical contact with objects within the blind visual field but seen only in the p-prisms is presumably a rare occurrence in everyday use. We propose that this lack of physical interaction might be the reason why adaptation did not occur in the Giorgi et al study.¹⁰ We hypothesize that perceptual-motor training requiring reaching for stimuli seen through the p-prism will produce motor-proprioceptive adaptation similar to the prism adaptation paradigm for yoked prisms (referred to as wedge prisms in traditional prism adaptation studies; see Kornheiser 1976 for a review).¹³ This motor adaptation should result in faster and more appropriate responses to hazards and improved visual comfort and acceptance rates.

This protocol paper describes the p-prism adaptation training protocol which is currently being used in an ongoing pilot study (to establish preliminary data for a future clinical trial). It is now common to publish such protocol papers ahead of the results.¹⁴⁻¹⁶ It is critical in this case because a novel

software and training method were developed that cannot be adequately described in a limited methods section of the pilot study paper.

Unlike other training regimens for hemianopia which aim to improve the visual field by restoration of vision, ^{17,18} this training was specifically designed to aid in adaptation to the p-prisms. Any effect is expected to be immediately eliminated when the p-prism glasses are removed, leaving at most a short-lived adaptation aftereffect. In addition to measuring the impact of the training on reaching accuracy for stimuli seen through the p-prisms, transfer of these skills to mobility-related tasks is being evaluated using a pedestrian detection task in a driving simulator, ^{23,24} collision judgments in the p-prisms in virtual shopping mall²¹ and gaze behaviours during outdoor walking²². The methods for the driving simulator pedestrian detection task have been described in detail elsewhere. ^{23,24} The collision judgment task and outdoor gaze tracking will be described in separate manuscripts currently in preparation.

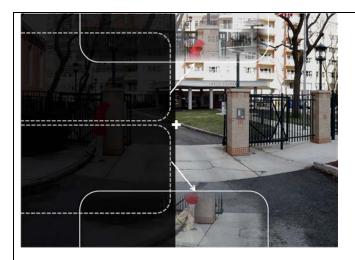


Figure 2 a) Simulation of the view through unilateral oblique 57Δ p-prisms in left hemianopia with fixation at the white cross. The left field is shaded to illustrate vision loss. The areas within the solid white lines represent the physical locations of the prism segments. The dashed lines outline the areas that are imaged by the oblique prisms. The 25-30° portion of the blind left field with the pedestrian is visible only to the left (prism)



b) Illustration of the predicted result of perceptual adaptation to p-prisms: the pedestrian is perceived in the veridical position/direction. Based on qualitative reports from pilot study and development experiment patients, the prism vision appears less clear than the intact vision, which is likely due to the inherent contrast reduction from the prism. This contrast reduction was illustrated here with reduced contrast in the portion of

eye. The right eye has no prisms and so sees the regular view (pedestrian not visible to right eye). This results in binocular rivalry in the prism area (illustrated as transparency), but no apical scotomas under binocular conditions, and no diplopia. The pedestrian is detected, but the location may be misinterpreted as being slightly to the right. If the patient is asked to point to the pedestrian without looking over, they point slightly right at the prism image.

the photo seen through the prisms (to the left of the fixation cross).

2.0 METHODS

Overview of Training Task

Patients fixate the center of a computer touch screen while targets are presented in the periphery of the screen. The patient is asked to touch the target while maintaining fixation centrally. With p-prisms, the perceived position of the target differs from its real position when presented in the prism expansion zones. Thus, before training, the patient will touch the apparent location (fig 3). The primary goal then is to train the patient to quickly touch the *real* position of the target when it appears in the prism expansion zones. Note that targets presented to the intact hemifield are seen in the correct direction with both eyes when presented in a prism free location, and are seen only by the non prism eye (and therefore in the correct direction) when presented in the area of the intact hemifield where the prism is sitting (targets are blocked from the view of the prism eye by the prism apical scotoma).² Direction is only misperceived when targets are presented to the blind hemifield within the prism expansion zones (fig 3 & 4).

Physical Set-up

The training station is composed of a 70cm x 40cm Surface Acoustic Wave touch screen, Windows computer, fixation monitoring camera, operator monitor, chinrest/headrest assembly, and adjustable height table and chair (Fig 3). The patient's head is held at 45 cm from the screen (closer or further away, if needed), a comfortable distance for reaching out to touch the screen. The eye to screen

distance is input into the software which automatically calculates and adjusts visual angles. Targets (peripheral stimuli which the patient should touch) are 30mm checkerboards (3.82°, 0.26cpd, ~20/900) presented from 200ms to 5000ms, depending on the training level. Screen backgrounds are plain gray, natural image photographs of walking or road scenes, or videos taken from the point of view of a car driver (extracted from driver training videos from the UK Hazard Perception Test²⁵ and reversed horizontally to present driving on the right side of the road).

Fixation stimuli are either a 15 mm fixation cross or a video file in a central display window used to increase cognitive load while making the session more engaging (see movie watching task, table 1). Fixation is monitored using a table-mounted webcam and probed by presenting catch trials into non-seeing areas. Minimizing eye movement is contrary to the manner in which the patients are instructed to use the prisms in everyday life (typically they are taught to look to the blind side to identify objects detected through the prisms). This contradiction is explained and reinforced throughout the training.

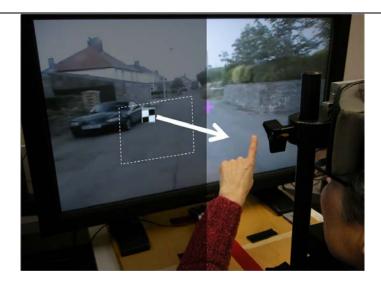


Figure 3. Participant training station illustrating a person with left HH performing a baseline trial. The checkerboard stimulus is presented over a video scene in the blind left hemifield (illustrated by shading) within an oblique prism (lower segment) expansion area (outlined by the dashed rectangle). The prism image of the checkerboard is shifted toward the seeing hemifield so that it appears to the patient as though on the right side of the screen, at the lower position pointed to by the arrow head (note: patient's hand is mid-reach, eventually ending at the tip of the arrowhead). The prism image results in an incorrect patient response (touching of the apparent position). The participant is unaware of their error since they see the real view of their finger (from the

non-prism eye) in the same direction as the prism image of the target. Even once they reach the screen and have visual feedback of their finger and the target, they are still unaware of their error since the smooth touch screen provides no tactile feedback. They continue to believe they are touching the correct location unless auditory feedback is given. Auditory feedback is only given during the training sessions, not during the *Performance Measure Task* used to measure the outcome of training.

Mapping the Visual Field and Zone Placement

The training software is also used to measure the central 90°H x 42°V of the visual field (fig 4). First, the visual field is mapped kinetically, using the 30mm checkerboard target, without and then with the pprisms (Goldmann Perimetry is performed at study intake). Next, zones (rectangular regions) are manually positioned, using the operator screen, within the areas of field expansion; one each for the upper and lower prism, and a "catch zone" outside the expansion area in the blind hemifield where no detection is expected (fig 4). The catch zone is positioned next to the prism zone such that eye movement into the blind field causes the catch zone to fall within the visible prism expansion area, producing a false positive. Upper, lower, and outer prism zone borders are set using kinetic presentation (non-seeing to seeing) by asking the patient when the target appears. The inner border (next to the seeing hemifield) is determined by presenting the target to the newly defined prism zone, moving it (kinetically) towards the midline, and having the patient report when they see 2 targets. Targets close to the middle of the screen (near the border of the field loss) are at risk for being seen in two different directions; one by the prism and the other by the non-prism eye, resulting in peripheral diplopia, which can be confusing during training. Placing the inner border further into the blind field prevents this. Once the prism zones are mapped and sized, they are confirmed with a static presentation to the four corners of the zone. Next, 3 seeing side zones are manually positioned within areas corresponding to the prism zones for a total of 6 zones where targets will be presented during training. Zones are verified at the start of each visit, and as needed during training. If changes in location or size are discovered, every effort is made to adjust the glasses or chinrest first, only changing the zone locations if necessary.

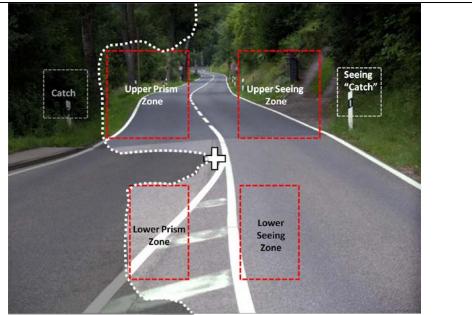


Figure 4: Photo illustration of the operator screen (37x28cm) showing zone placement for a patient with left HH wearing oblique p-prisms. Using kinetic perimetry, the operator marks the border of the field on the prism-side (dashed white line), while the patient fixates the white cross, and then draws the borders of the prism zones (dashed rectangles). The catch zone is set in an area of the blind hemifield where detection is not expected (upper left). There are also 3 seeing side zones corresponding to each prism zone.

Touch Response Measures

Reaction times (from stimulus onset to screen touch), and inaccuracy (distance of the touch location from the center of the target) are recorded by the software.

Feedback

During training, immediate audio feedback is given by the software following each screen touch. Three different sounds are used for 1) a correct touch (within 4°), 2) a same side miss (>4° touch inaccuracy, but on the correct side of the screen), and 3) a wrong side miss (reached for the prism image on the opposite side of the screen). Four degrees was used based on development experiments with normally sighted which found fixed gaze accuracy + 1SD =3.4°. The meaning of the audio feedback is explained to the patients. Descriptive statistics of performance are output at the end of each training session on the operator's screen, and a simplified version on the patient screen with success rate for target

accuracy (within 4°) and an animated GIF character providing feedback such as "good job or almost there, etc."

Primary Performance Measure

A primary performance measure task was developed and implemented at baseline (before training), and at the beginning and midway point of each training visit. In early pilot testing, fatigue was apparent by the end of the visit and so a mid-visit performance measure was preferred as being more representative of within visit learning. It uses 10 presentations in each zone (and 2 in each catch zone) to measure the retention of training from the previous visit and to monitor within-visit progress. The stimulus remains on the screen for 1500ms and time between presentations varies from 1000-1950ms. There is no audio feedback other than a beep indicating the screen has been touched. Patients are kept naïve to their performance on the task.

Visual Open Loop Performance Measure

The visual open loop performance measure task uses a flash presentation (200ms) so the stimulus and finger cannot be seen at the same time, and thus visual feedback cannot be used to guide reaching.

Patients are tested (10 trials to each prism zone) with the prism side hand, and then with the seeing side hand to measure intermanual transfer (IMT, see discussion section for explanation).

Participants for Pilot study

Participants are being recruited from Ophthalmology, Optometry, and Physical Medicine practices within the Greater Boston area, and also from a database search at Massachusetts Eye and Ear Infirmary for patients with a diagnosis of homonymous field defect. Inclusion criteria are complete HH defined as ≤5° of residual vision on the hemianopic side of the vertical meridian within 20° above and below fixation assessed with a Goldmann V4e,¹⁰ at least 14 years of age, >3months since HH vision loss, Mini-Mental Status Examination ≥24²⁶, no hemispatial neglect (Schenkenberg Line Bisection test ²⁷ and Bells test ²⁸), best corrected visual acuity 6/15 (20/50) or better in each eye, no strabismus (when wearing spectacles), ability to walk or self ambulate wheelchair, no severe vertigo or vestibular

dysfunction, no history of seizures in prior 3 months, and willingness to wear p-prisms and attend 15-19 visits (including assessments, prism fitting and dispensing, and 6 sessions of training).

All participants receive permanent 57Δ oblique p-prisms glasses fitted using methods described in detail elsewhere.⁵

The study is being conducted in accordance with the tenets of the Declaration of Helsinki.

Informed consent is obtained from the participants after explanation of the nature and possible consequences of the study. The protocol was approved by the institutional review board at the Massachusetts Eye and Ear Infirmary and the U.S. Army Medical Research and Material Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO).

Typical training visit

A typical training visit is comprised of baseline performance measure tasks (without feedback), a review of previous levels or concepts, training with audio feedback of touch inaccuracy and coaching from the experimenter, repeat of the performance measure tasks, a 15-minute break, additional practice (as needed), and an introduction to the next level. Patients complete 8-12 individual sessions (defined as one run of a particular task) per visit (typical session length is 4-5 minutes). The visit is approximately an hour with multiple 1-2 minute rest periods between sessions. Typical total training time (where the patient is actively touching the screen) is approximately 30 minutes/visit.

Training Protocol

This section reports the training protocol now being used in the pilot study.

Level 1

Level 1 promotes motor adaptation of the prism-side hand. Targets are <u>only</u> presented to the blindside prism zones, speed is not emphasized (5 s stimulus duration), and only the prism-side hand is used. Patients are taught to sweep their hand into the blind side and detect it within the prism, align the hand with the target (also seen in the prism), and touch it. This provides visual feedback in addition to the auditory feedback described above. Fifty or more presentations are made in each zone (typical for

prism adaptation experiments²⁹) and targets are the 30mm square checkerboards (increased to 40mm if detection is poor). Video backgrounds are used unless detection is poor, in which case solid gray backgrounds are used first. In addition, there is an option for manual presentation of targets under experimenter control for cases where performance is initially very poor. The criterion for passing level 1 is 80% detection and inaccuracy of no more than ±4° on the level 1 task.

Level 2

The objective is to learn to discriminate targets appearing in the prism zones from those on the seeing side. The patient is instructed to notice the relative "blurriness" of the 30mm checkerboard target seen through the prism and once they can distinguish "prism vision" and "regular vision", they complete 100 training trials in which 30mm checkerboard targets are presented randomly to all zones. The following instructions are given: "First decide if the stimulus is in the prism or your regular vision. If it is in the prism, use the hand on that side (blind side) to reach into the prism vision as you did in level 1. If it is on your seeing side, just reach and touch normally with the hand on that side. Go slow and make sure you keep your eye on the center fixation target." Level 2 is completed when no more than ±4° inaccuracy and 80% detection rate are exhibited on the prism (blind) side

Level 3

The objective is to decrease the prism side reaction time to approach that of the baseline seeing side, while maintaining $\leq \pm 4^{\circ}$ inaccuracy and at least 80% detection. The training trials are identical to level 2, except that stimulus duration is gradually reduced, depending on seeing side performance, from ~5s to ~1s. The minimum criterion for passing level 3 is prism side reaction time not more than twice the reaction time on the seeing side.

Level 4

The objective is to increase cognitive load and improve detection of natural hazards within natural scene images and videos (sublevel 4.3). Level 4 includes 3 sub-tasks: 4.1 *stop-go* (refrain from making screen touches when the fixation cross is red); 4.2 *divided attention movie watching* (video clips played at the center of the display; the remainder of the background is a static image); and 4.3 *hazard*

detection (videos from the driver's perspective played over the entire screen in which hazards repeatedly enter the vehicle's path from the prism side). In sublevel 4.3, patients maintain fixation on the cross and tap the table with a stylus when the hazard is first detected in the prism. Sublevel 4.3 is different from the other levels since the targets are actual hazards within the video background (ie. pedestrians in a crosswalk), and so of much lower contrast than the checkerboard targets used in all other levels. As a result, higher resolution and/or better awareness of the p-prism vision are needed. The subject is taught to tuck their chin in while maintaining fixation on the central cross. This moves the upper prism closer to the line of sight and the prism image to a smaller retinal eccentricity, improving resolution and enhancing detection. It is explained how this can be done in everyday life, not just during the training. They are carefully instructed not look directly into the prism. Once hazards are consistently detected, they are instructed to touch the screen where the hazard first appeared (the hazards are moving towards the path of movement). Level 4 is completed when the hazard location is touched 80% of the time before it crosses into their intact visual field.

Level 5

This level was designed to promote perceptual adaptation through verbal reinforcement of true target location and by calling attention to shifted parts of the background scene. This scene-shift-feedback is the type of visual feedback available in every-day use of the p-prisms where obstacles to be detected are frequently beyond arm's reach. Baseline for this task is measured by asking the patient to verbally report whether a target appears to the right or left of a human figure positioned in the center of a background photo. The experimenter records the response (no touch is made initially). The targets and portion of the background within the p-prism view are imaged (retinotopically) on the opposite side of the human figure than where they are truly located, but if perceptually adapted or applying a cognitive correction, patients may accurately report location. They are then asked to touch the targets while saying "right" or "left", with feedback being provided by the software in the same manner as other levels. Level 5 is complete when reaching inaccuracy is no more than ±4° with at least 80% correct verbal responses.

Table 1: Perceptual-Motor Training Levels

Level	Description	Goal
1	Targets in the prism only	≤ ±4° inaccuracy (median)
2	Learn to discriminate prism & seeing side targets	Maintain ≤ ±4° inaccuracy
3	Improve reaction time by reducing stimulus duration	Maintain ≤ ±4° inaccuracy and reduce prism zone response time to ≤ 2x seeing side
	4.1 Stop-Go Task	Improve detection of roadway hazards within natural
4	4.2 Movie Watching	driving scenes to 80% correct localization. Focuses on
	4.3 Hazard Detection	improvement in performance under cognitive loading
		Verbalize correct target location (even if perceived
5	Perceptual Training	incorrectly) with ≤ ±4° inaccuracy and at least 80%
		correct responses. Use components of the background scene to code target location in far space
		ossile to osse target location in lar opace

RESULTS

To illustrate the development of the training protocol and the practical use of the software, we first report detailed results for a participant who completed a preliminary version of the protocol during the development phase. We then report preliminary results for the ongoing pilot study.

Participant who completed the protocol during development

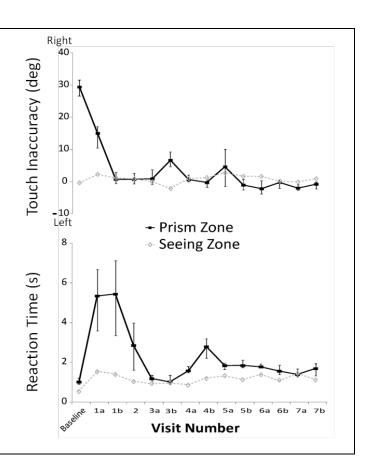
S was an 18 year-old survivor of a right posterior communicating artery aneurysm repair with post-surgical ischemia resulting in left homonymous hemianopia (HH) meeting the inclusion criteria. Baseline touch inaccuracy, measured before instruction, showed a predictable 30° rightward and downward error equal to the prism displacement (fig. 5, upper panel). S had no idea his performance was poor (no learning effect evident on the primary outcome measure (performance measure task)).

Baseline reaction times were fast because *S* quickly reached to the target's apparent position (fig. 5, lower panel, baseline data point).

To demonstrate the reaching error to S we showed him the target's position while he kept his finger pointed to its location perceived through the prism. Now aware of his error, we trained him to compensate by swinging his left arm far out to the left (blind) side and slowly bringing it towards midline until it was visible to him through the prism (but not within his intact right hemifield), lining it up with the target (checkerboard), and touching it (practiced 10 times). Next, we demonstrated the difference in appearance of the target when it was in the prism (blurry, horizontally compressed, colored fringes) compared to his prism free vision. He understood this quickly and discriminated easily without practice. Afterwards, we began the training tasks.

In the first session, a 5s stimulus duration was given to allow time to perform the left hand sweeping technique, which worked well resulting in a highly reduced inaccuracy (+1.5°; fig., upper panel, data point 1b) but with a long response time. He had some improvement in response times at visit 2 (reduced to 3s), but was becoming frustrated. At visit 3, we began by prism adapting the left hand prior to requiring target reaching with the right hand, which was helpful (level 1 in the final protocol). We were able to increase his speed of reaching to about 1 s, identical to the seeing side, and encourage abandonment of the sweeping strategy. By visit 6 performance improvements were sustained between visits. Furthermore *S* reported, at times, a continuous perception of his vision as if he had perceptually adapted in addition to the motor adaptation measured by the software.⁸⁸

Figure 5: Median touch inaccuracy (upper panel), and response times (lower panel) over 4 weeks of training for pilot participant S with left HH. As the bases of the pprisms were to the left, images were shifted rightward, resulting in a rightward (positive) reach inaccuracy at baseline for targets in the prism zone, which rapidly improved in a few visits (upper panel). Reaction times were much longer during visits 1a, 1b, and 2 (lower panel) while top-down strategies were employed to improve touch accuracy (upper panel). However, by the end of training, touch accuracy and reaction times were similar in the prism and seeing zones. Error bars represent the interquartile range for the prism zone data.



Ongoing pilot study

A total of 19 patients have been enrolled in the pilot study (July 2011 to November 2013) of which 5 withdrew, citing declining health (n=2) and too many visits (n=3). Of those who have completed training (n=14) mean age is 51, 79% male, 100% Caucasian, 64% have left HH, and none had prior experience with p-prisms.

Table 2: Patient characteristics					
<u>(n=14)</u>	<u>Mean</u>	Range			
Age	51yrs	(18yrs-82yrs)			
Female	21%	NA			
Left HH	64%	NA			
Time since vision loss	4.3yrs	(0.25yrs-15yrs)			
MMSE (max 30)	26	(24-30)			
Self-Reported Mobility Score (best is 55)	20	(12-27)			
Type of Cerebrovascular Accident	Ischemic (57%)	NA			
	Aneurysm (29%)				

Preliminary results from this training protocol (n=7, mean age 53, 71% male, 100% Caucasian, 57% left HH) were presented,³⁰ and found touch accuracy error to targets presented in prism areas improved significantly (Wilcoxon p=0.02) from median (H,V) (17°, 6°) at baseline to (1°, 0.5°) at the end of training (equivalent to seeing-side accuracy). The median difference between seeing and prism side reaction times reduced significantly (Wilcoxon p=0.04) from 880ms to 110ms.

DISCUSSION

Outcome measures: The primary performance measure task evaluates the overall ability of patients to detect, discriminate prism from seeing side targets, and quickly and accurately touch targets presented over natural driving scene videos. Since this is most similar to a real-world situation, it is an important primary outcome measure. However, it cannot distinguish whether poor performance was a consequence of poor discrimination or failure to achieve sensorimotor adaptation, and tells us nothing about the locus or mechanism of adaptation. For this we developed a visual open loop task similar to that used in traditional voked prism adaptation studies^{29, 31} but with some important differences. Similar to traditional prism adaptation, it eliminates visual feedback during the reach and masks success for target acquisition, making failure to adapt more apparent. In traditional prism adaptation, visual open loop aftereffects were larger and more resistant to decay than closed loop, 29 presumably as a consequence of the lack of visual feedback. By having a plain gray background, the task maximizes the likelihood of detection and reduces allocentric scene-shift cues which might be used strategically. It also eliminates the discrimination factor (targets only appear in the p-prism zones), and is sufficiently different from the training task to provide some measure of generalization. Unlike a traditional visual open loop paradigm, it is performed when wearing the prisms and so is not measuring an aftereffect. In fact, an aftereffect cannot be measured in p-prism adaptation because without the p-prisms the target is in the hemianopic field where it cannot be detected. Traditional prism adaptation results in a change in the felt position of the eyes and/or head (ocular proprioception)^{13, 29} but this is not expected in p-prism

adaptation since gaze is fixed and head immobilized during training. Instead we look for evidence of change in visual coordinates (visual adaptation) using intermanual transfer ³²⁻³⁴ and the collision envelope; where patients make a purely visual collision judgment with a human figure in a virtual shopping mall corridor, the methods for which are reported elsewhere. ^{21, 35, 36} Absence of intermanual transfer and/or failure to show improvements in collision judgment would provide evidence against visual adaptation. ^{13, 32-34} However, the presence of intermanual transfer (accurate reaching with the untrained seeing side arm) and improved collision judgments (prism collision judgments similar to regular vision collision judgments) does not rule out strategic cognitive correction.

Encouraging the Use of Strategies (levels 1 and 2): A strategy of sweeping the arm out to the blind side was advocated in levels 1 and 2. Traditional prism adaptation studies suggest that increasing strategic components (recalibration) reduces the sensorimotor realignment (i.e. true adaptation). An important distinction is that this training protocol is much longer in duration than traditional prism adaptation protocols. The realignment mechanisms are targeted in levels 3, through 5. Because of the large 30° p-prism deviation, some level of strategy was needed to achieve progress.

Discriminating Prism Targets by Prismatic Blur (level 2): Accurate level 2 performance (targets presented to both sides of the screen) requires development of two representations of physical space for targets appearing in the same visual direction. Fortunately there are multiple reports suggesting this type of adaptation is possible. Such development is likely to be initially strategic (cognitive, or topdown); i.e. blurry targets are in the prism and need to be touched with the blind side hand. Using blur as a cue is potentially problematic; it introduces attentional demand and lengthens reaction times, and so is being closely monitored in the pilot study.

Equalizing Blind and Seeing Side Reaction Times (levels 3 and 5): Fast reaching and abandonment of strategies is crucial to both achieving head-centered realignment (non-strategic adaptation characterized by realignment of sensory motor systems)⁴⁰ and the fast reactions needed to avoid hazards in everyday life. Getting subjects to reach quickly was not trivial. Experimenters needed to encourage subjects and emphasize that "some mistakes were ok". Perceptual Training (level 5):

Although attending to background cues may help localization and perceptual adaptation, background cues are often ignored, a form of inattentional blindness.⁴⁵ Qualitative reports by pilot subjects suggested that mandating attention to the background helped them use the cues. Verbalizing target location while reaching may link the motor action with the perceptual response and lead to the visualization needed for perceptual adaptation.

CONCLUSION

Decades of prism adaptation studies suggest p-prism adaptation should be possible when combined with an active task. 8, 11, 12 A prior p-prism study 10 did not measure adaptation like that documented in split prism studies with extended full time binocular wear, 8, 9 so we developed this formal training regimen. An ongoing pilot study is using this training software and protocol and aims to determine preliminary efficacy as well as look for any evidence of transfer to everyday mobility tasks in a group of patients learning to use p-prisms.

REFERENCES

- 1. Peli E. Field expansion for homonymous hemianopia by optically-induced peripheral exotropia. *Optom Vis Sci.* 2000;77:453-464.
- 2. Apfelbaum HL, Ross NC, Bowers AR, Peli E. Considering apical scotomas when prescribing prisms for homonymous hemianopia. *Translational Vision Science & Technology.* 2013;2:2, http://tvstjournal.org/doi/full/10.1167/tvst.1162.1164.1162.
- 3. Peli E, inventor. Peripheral field expansion device. United States patent US 7,374,284 B2. 2008 May 20, 2008.
- 4. Jung J-H, Peli E. Impact of high power and angle of incidence on prism corrections for visual field loss. *Opt Eng.* 2014; doi: 10.1117/1.OE.53.6.061707;53.
- 5. Bowers AR, Keeney K, Peli E. Community-based trial of a peripheral prism visual field expansion device for hemianopia. *Arch Ophthalmol.* 2008;126:657-664.
- 6. Bowers AR, Keeney K, Peli E. Randomized Crossover Clinical Trial of Real and Sham Peripheral Prism Glasses for Hemianopia. *JAMA Ophthalmology*. 2014;132:214-222.
- 7. O'Neill EC, Connell PP, O'Connor JC, Brady J, Reid I, Logan P. Prism therapy and visual rehabilitation in homonymous visual field loss. *Optom Vis Sci.* 2011;88:263-268.
- 8. Kohler I. The formation and transformation of the perceptual world. *Psychol Issues*. 1964;3:14-173
- 9. Pick HL, Jr., Hay JC, Martin R. Adaptation to split-field wedge prism spectacles. *J Exp Psychol.* 1969:80:125-132.
- 10. Giorgi RG, Woods RL, Peli E. Clinical and laboratory evaluation of peripheral prism glasses for hemianopia. *Optom Vis Sci.* 2009;86:492-502.

- 11. Held R, Hein A. Adaptation of disarranged hand-eye coordination contingent upon re-afferent stimulation. *Percept Mot Skills*. 1958;8:87-90.
- 12. Fernández-Ruiz J, Díaz R, Aguilar C, Hall-Haro C. Decay of prism aftereffects under passive and active conditions. *Cogn Brain Res.* 2004;20:92-97.
- 13. Kornheiser A. Adaptation to laterally displaced vision: a review. *Psychol Bull.* 1976;83:783-816.
- 14. Stelmack JA, Tang XC, Reda DJ, Stroupe KT, Rinne S, Massof RW. VA LOVIT II: a protocol to compare low vision rehabilitation and basic low vision. *Ophthalmic Physiol Opt.* 2012;32:461-471.
- 15. George S, Hayes A, Chen C, Crotty M. The effect of static scanning and mobility training on mobility in people with hemianopia after stroke: a randomized controlled trial comparing standardized versus non-standardized treatment protocols. *BMC neurology*. 2011;11:87, 81-86.
- 16. Dunbar HM, Crossland MD, Bunce C, Egan C, Rubin G. The effect of low vision rehabilitatin in diabetic eye disease: a randomised controlled trial protocol. *Ophthalmic Physiol Opt.* 2012;32:282-293.
- 17. Huxlin KR, Martin T, Kelly K, et al. Perceptual relearning of complex visual motion after V1 damage in humans. *J Neurosci.* 2009;29:3981-3991.
- 18. Sabel BA, Kenkel S, Kasten E. Vision restoration therapy (VRT) efficacy as assessed by comparative perimetric analysis and subjective questionnaires. *Restor Neurol Neurosci.* 2004;22:399-420.
- 19. Peli E, Bowers AR, Mandel AJ, Higgins K, Goldstein RB, Bobrow L. Design of driving simulator performance evaluations for driving with vision impairments and visual aids. *Transport Res Record: J Trans Res Board.* 2005;1937:128-135.
- 20. Bowers AR, Mandel AJ, Goldstein RB, Peli E. Driving with hemianopia: 1. Detection performance in a driving simulator. *Invest Ophthalmol Vis Sci.* 2009;50:5137-5147.
- 21. Houston KE, Churchill JH, Luo G, Woods RL, Peli E, Bowers AR. Peripheral prism glasses for hemianopia improve obstacle detection during virtual walking (abstract). *Optom Vis Sci.* 2012;89:E-abstract 120979.
- 22. Tomasi M, Churchill JH, Wiegand J, et al. Peripheral prisms increase blindside eye and head scanning movements during outdoor walking in hemianopes: preliminary results (abstract). *Investigative Ophthalmological & Visual Science*. 2013.
- 23. Bronstad PM, Bowers AR, Albu A, Goldstein RB, Peli E. Driving with central visual field loss I: Effect of central scotoma on response to hazards. *JAMA Ophthalmology*. 2013;131:303-309.
- 24. Alberti CF, Peli E, Bowers A. Driving with hemianopia: III. Detection of stationary and approaching pedestrians in a simulator. . *Invest Ophthalmol Vis Sci.* 2014;55:368-374.
- 25. Driving test success: hazard perception. Rugeley, UK: Focus Multimedia Limited; 2002-2009.
- 26. Folstein MF, Folstein SE, McHugh PR. Mini-Mental State: A practical method for grading the cognitive status of patients for the clinician. *Journal of Psychiatric Research.* 1975;12:189-198.
- 27. Schenkenberg T, Bradforn DC, Ajax ET. Line bisection and unilateral visual neglect in patients with neurologic impairment. *Neurology.* 1980;30:509-517.
- 28. Vanier M, Gauthier L, Lambert J, et al. Evaluation of left visuospatial neglect: Norms and discrimination power of two tests. *Neurology*. 1990;4:87-96.
- 29. Redding GM, Wallace B. Adaptive Spatial Alignment. Mahwah, NJ: Erlbaum; 1997.
- 30. Houston KE, Churchill JH, Wiegand J, et al. Is perceptual-motor adaptation in hemianopes wearing peripheral prisms possible? Pilot study preliminary results. (Abstract). *Investigative Ophthalmological & Visual Science*. 2013;313.
- 31. Wilkinson DA. Visual-motor control loop: A linear system? J Exp Psychol. 1971;89:250-257.
- 32. Harris CS. Perceptual adaptation to inverted, reversed, and displaced vision. *Psychol Rev.* 1965;72:419-444.
- 33. Cohen MM. Continuous versus terminal visual feedback in prism aftereffects. *Percept Mot Skills*. 1967;24:1295-1302.

- 34. Redding GM, Wallace B. Asymmetric visual prism adaptation and intermanual transfer. *J Motor Behav.* 2009;41:83-94.
- 35. Apfelbaum HL, Pelah A, Peli E. Heading assessment by "tunnel vision" patients and control subjects standing or walking in a virtual reality environment. *ACM Transactions on Applied Perception (TAP)*. 2007;4:1-15.
- 36. Luo G, Woods RL, Peli E. Collision judgment when using an augmented-vision head-mounted display device. *Invest Ophthalmol Vis Sci.* 2009;50:4509-4515.
- 37. Redding GM, Wallace B. Calibration and alignment are separable: Evidence from prism adaptation. *J Motor Behav.* 2001;33:401-412.
- 38. Redding GM, Wallace B. Strategic calibration and spatial alignment: A model from prism adaptation. *J Motor Behav.* 2002;34:126-138.
- 39. Redding GM, Wallace B. Cognitive load and prism adaptation. *J Motor Behav.* 1992;24:238-246
- 40. Redding GM, Wallace B. Effects of pointing rate and availability of visual feedback on visual and proprioceptive components of prism adaptation. *J Motor Behav.* 1992;24:226-237.
- 41. McGonigle BO, Flook J. Long-term retention of single and multistate prismatic adaptation by humans. *Nature*. 1978;272:364-366.
- 42. Welch RB, Bridgeman B, Anand S, Browman KE. Alternating prism exposure causes dual adaptation and generalization to a novel displacement. *Percept Psychophys.* 1993;54:195-204.
- 43. Redding GM, Wallace B. Dual prism adaptation: calibration or alignment? *J Motor Behav.* 2003;35:399-408.
- 44. Miyauchi S, Egusa H, Amagase M, Sekiyama K, Imaruoka T, Tashiro T. Adaptation to left-right reversed vision rapidly activates ipsilateral visual cortex in humans. *Journal of Physiology Paris*. 2004;98:207-2019.
- 45. Apfelbaum HL, Gambacorta C, Woods RL, Peli E. Inattentional blindness with same scene at different scales. *Ophthalmic Physiol Opt.* 2010;30:124-131.